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Criteria to clear polytrauma patients with traumatic brain injury for safe definitive surgery (<24 h)

Yannik Kalbas [a,b,1,*], Yannik Stutz [b,1], Felix Karl-Ludwig Klingebiel [a,b], Sascha Halvachizadeh [a], Michel Paul Johan Teuben [a], John Ricklin [b], Ivan Sivriev [b], Jakob Hax [c], Carlos Ordonez Urgiles [b], Kai Oliver Jensen [a], Markus Florian Oertel [d,e], Hans-Christoph Pape [a,b], Roman Pfeifer [a,b]

[a] Department of Trauma Surgery, University Hospital Zurich, University of Zurich, Rämistrasse 100, 8091 Zurich, Switzerland
[b] Harald-Tscherne Laboratory for Orthopaedic and Trauma Research, University Hospital Zurich, University of Zurich, Rämistrasse 100, 8091 Zurich, Switzerland
[c] Department of Hip and Knee Surgery, Schulthess Clinic, Lengghalde 2, 8008 Zurich, Switzerland
[d] Department of Neurosurgery, University Hospital Zurich, University of Zurich, Rämistrasse 100, 8091 Zurich, Switzerland
[e] Clinical Neuroscience Center, University Hospital Zurich, University of Zurich, Rämistrasse 100, 8091 Zurich, Switzerland

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ABSTRACT

Introduction: Optimizing treatment strategies in polytrauma patients is a key focus in trauma research and timing of major fracture care remains one of the most actively discussed topics. Besides physiologic factors, associated injuries, and injury patterns also require consideration. For instance, the exact impact and relevance of traumatic brain injury on the timing of fracture care have not yet been fully investigated.

Methods: In this retrospectively cohort study at a level one trauma center, patients requiring trauma team activations from 2015 to 2020 were screened. Patients with an injury severity score >16 and at least one body region requiring operative fixation were included. Patients who underwent their first definitive surgery <24 h were stratified as group SDS (Safe Definitive Surgery) and >24 h as group DFC (Delayed Fracture Care). Outcomes were early mortality (<72 h), SIRS and sepsis, timing to first definitive surgery and completed reconstruction, total number of surgeries, and factors influencing the surgical strategy (e.g., unstable physiology). Odds ratios for treatment strategies and influencing factors were calculated using the Fisher`s exact test with conditional maximum likelihood estimate.

Results: From a total of 901 patients screened, 239 were included in the analyzes (Group DFC: 151, Groups SDS: 88). Groups did not significantly differ regarding early mortality, SIRS and sepsis. Group SDS had a significantly lower mean number of operations (4.3 vs. 5.3; $p = 0.037$) and a significantly shorter mean time until completion of reconstructive operations (10 days vs. 15 days; $p = 0.013$). Unstable physiology and intracranial trauma sequelae with the necessity for neurosurgical interventions (NSI) were identified as most significant factors for delaying definitive fracture care (OR: 2.85; 95 % CIs: 1.56 to 5.33 and OR: 5.59; 95 % CIs: 1.63 to 29.85), while the presence of intracranial bleeding (IB) without NSI did not have a significant influence (OR: 1.21; 95 % CIs: 0.63 to 2.34).

Conclusion: The necessity of NSI and unstable physiology are highly relevant factors for delaying definitive fracture care in polytrauma patients, while the presence of IB without NSI had less impact. In this cohort, early definitive fracture care in physiologically stable patients without NSI, was not associated with increased patient morbidity.

* Corresponding author.
E-mail addresses: yannik.kalbas@usz.ch (Y. Kalbas), yannik.stutz@gmail.com (Y. Stutz), felixkarl-ludwig.klingebiel@usz.ch (F.K.-L. Klingebiel), sascha.halvachizadeh@usz.ch (S. Halvachizadeh), michel.teuben@usz.ch (M.P.J. Teuben), john.ricklin@gmail.com (J. Ricklin), ivan.sivriev@usz.ch (I. Sivriev), jakob@hax.de (J. Hax), carlos.ed.ord@gmail.com (C.O. Urgiles), kaioliver.jensen@usz.ch (K.O. Jensen), markus.oertel@usz.ch (M.F. Oertel), hans-christoph.pape@usz.ch (H.-C. Pape), roman.pfeifer@usz.ch (R. Pfeifer).
[1] Contributed equally.

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Abbreviations

cCT	Cranial computed tomography
DFC	Delayed fracture care
GCS	Glasgow coma scale
IB	Intracranial bleeding
ICP	Intracranial pressure
ISS	Injury severity score
IQR	Interquartile range
MLS	Midline shift
MuST	Musculoskeletal temporary (Surgery)
NSI	Neurosurgical intervention
TBI	Traumatic brain injury
SIRS	Systemic inflammatory response syndrome
SD	Standard deviation
SDS	Safe definitive surgery
95%CIs	95% Confidence intervals
OR	Odds ratios

Introduction

Physical trauma continues to be a prominent cause of fatalities and impairments, worldwide particularly among young men[1]. High-energy traumata, such as falls from great heights and motor vehicular accidents can induce a potentially lethal combination of blood loss, traumatic brain injury (TBI), soft tissue damage, and major fractures, which may require immediate surgical intervention. Uncontrollable hemorrhage and severe TBI remain the most common causes of death, while major fractures and soft tissue trauma are significant causes of prolonged hospitalization, complications, and disability[2].

Timely definitive major fracture care has been repeatedly shown to lead to improved outcomes[3,4]. Defining criteria to clear multiply injured patients for early definitive major fractures care has long been a key focus of trauma research and several algorithms have been proposed [5–9].

Among them, there is considerable agreement on the importance the patients' physiological response to trauma and hemorrhage[6,10]. The introduction of targeted resuscitation protocols has enabled accelerated definitive surgery, even in patients, who are initially physiologically compromised[11]. Another factor that has historically been of high importance is the presence of chest trauma, especially in patients with long bone fractures to be treated with intramedullary reaming and nailing[12]. Additionally, soft tissue injury is highly relevant for the timing and sequence of fracture care, even in physiologically compensated patients. In these cases, the application of temporary fixation has been termed "MusculoSkeletal Temporary (MuST) surgery"[13].

While these factors have been extensively studied, categorized, and described in the literature, the importance of TBI on timing and sequence of fracture care is less well explored. A recent effort from our group has shown that the presence of severe TBI constitutes an important factor to delay definitive fracture care in polytrauma patients, independent of the physiological response[14]. Nonetheless, the extent of TBI is usually clinically graded by the Glasgow Coma Scale (GCS), which can be influenced by multiple and different conditions[15]. In this regard, the aim of this study, was to investigate to exact impact and relevance of traumatic brain injury on the timing of fracture management in polytrauma patients, with a focus on clearly objectifiable findings from cranial computed tomography (cCT). The following research questions were defined:

- What are significant factors to delay fracture care in polytrauma patients and is the timing of fracture care associated with the outcome?
- Does the presence of intracranial bleeding (IB) and the need for neurosurgical intervention (NSI) influence the timing of definitive fracture care and which types of IB are more likely to delay definitive fracture care?
- Is it possible to transfer the data from this retrospective analysis into criteria that assess polytrauma patients with traumatic brain injury for early definitive fracture care?

Methods

The reporting of this retrospective cohort study is in strict adherence with the STROBE guidelines. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (BASEC-Nr. 2020-00703).

Setting and participants

This study was conducted at a single Swiss Level I trauma center. Patients who were hospitalized from 2015 to 2020 with trauma team activation (suspected polytrauma, high-energy mechanism) were screened for eligibility.

Inclusion criteria

- An Injury Severity Score (ISS) >16 with at least two injured body regions
- At least one body region that required operative intervention (aside from the placement of chest tubes)
- Written consent for retrospective data analysis (in form of our hospital's general consent form)
- Complete data sets
- ≥16 years of age

Exclusion criteria

- Injuries to only one body region (regardless of ISS)
- Definitive treatment of all injuries during the initial surgery (Early Total Care)
- Transfer from another hospital (unless immediate referral after initial diagnostics)
- Death in the course of initial trauma bay treatment

Study group allocation

The primary objective of this study was to identify factors that drive surgical treatment decision towards early (<24 h) or delayed fracture care. Patients were allocated to two study groups based on the timing of the first definitive operative intervention[7]. The placement of Chest Tubes was not counted for either treatment strategy.

Group SDS (Safe Definitive Surgery) included patients who received at least one (not lifesaving) definitive operative intervention (almost exclusively fixation of major fractures) within the first 24 h.

Group DFC (Delayed Fracture Care) included patients, for whom definitive care was delayed by at least 24 h. This included patients who received damage control orthopedics (DCO) or MusculoSkeletal Temporary (MuST) Surgery. The interventions in this group included predominantly the placement of external fixators, but also extension, traction, splinting, or other damage control techniques (e.g., placement of negative pressure wound therapy for open abdomen treatment).

Outcomes and parameters

After allocation to the treatment groups, our primary outcome parameters were early mortality (<72 h) and the development of systemic inflammatory response syndrome (SIRS) and sepsis during the initial hospitalization. Secondary outcomes were procedural characteristics including time to first operation and completed reconstruction, and the total number of operations.

Further parameters were demographics, injury pattern, and severity, physiological stability, the necessity for life saving interventions, presence, and severity of chest injury, presence of relevant soft tissue injury (including open fractures and neurovascular injury), and the presence and degree of TBI as well as detailed information about the type of IB and the necessity for NSI.

Definitions

Damage Control Orthopedics (DCO) was defined as a delay of definitive fracture care due to systemic compromise (e.g., unstable physiology).

MusculoSkeletal Temporary (MuST) Surgery was defined as the delay of definitive fracture care due to soft tissue injury, as previously published by our group[13].

Early Total Care was defined as performing all required definitive interventions within the initial operation. This accounts mostly for patients with spinal fractures with associated cord injury, who require immediate decompression and stabilization but no additional fixation of other body regions. These patients were excluded from our final analyzes.

Unstable Physiology was defined as the presence of hemorrhagic shock (HS), relevant coagulopathy, severe hypothermia, and/or the necessity for lifesaving surgery (see below)[16]. Corresponding parameters have been previously summarized in a recent work from our group[17]. HS was diagnosed by a positive shock index in combination with a systolic blood pressure < 90 mmHg and a lactate > 2 mmol/l, or the need for transfusion of red blood cells. Coagulopathy was diagnosed based on the necessity for factor- or platelet transfusion.

Lifesaving surgery was defined as thoracotomy (anterolateral/bilateral), laparotomy, or pelvic packing for hemorrhage control.

Relevant chest injury was defined as an AIS ≥ 3 and/or the necessity for the placement of a chest tube.

Relevant soft tissue injury was defined as the presence of an Type II / III open fracture according to Gustilo-Anderson[18], injury to neurovascular structures, the presence of compartment syndrome, and signs of severe soft tissue compromise, such as blisters and/or pronounced swelling.

Major Fractures were defined as fractures to the spine, pelvis, long bone shafts, and displaced or comminuted intraarticular fractures of the upper and lower extremity[12,19].

Neurosurgical Intervention was defined as any emergency operation on the brain, including the insertion of external ventricular drainages or invasive multimodal neuromonitoring, and craniotomies for hematoma evacuations or decompressive craniectomies. The indications for these were made individually in a summary of anamnestic data, clinical and neuroradiological findings such as GCS (<9) and pupil status, relevant intracranial masses, signs of midline shift (MLS) > 5 mm and brain herniation, penetrating TBI and open or depressed skull fractures, as well as the documented or presumed patient's will[20].

SIRS and Sepsis were diagnosed by the treating intensive care unit physicians based on the widely accepted criteria, based on body temperature, heart rate, tachypnea, and white blood cell count as well as acute organ dysfunction (sequential organ failure assessment score) and the detection of pathogens.

Data extraction

Patients were identified in the clinical information system through the in-house data management and patient data was exported. Then, patient files were assessed individually, and additional information was extracted by two of the authors (YS & YK) from the respective reports (e.g., "trauma protocol", operative reports) and from radiographic and photographic imaging. Data was organized and stored in Microsoft Excel tables on password secured in-house computers.

Bias and study size

To achieve the maximal available study size and to minimize selection bias, all consecutive patients within the study period were screened for eligibility. As treatment-strategy could be influenced by patient and injury-specific factors, heterogeneity between the groups was expected. Data analysis was blinded.

Data analysis

Continuous, normally distributed data were presented as mean and standard deviation (SD). Non-normally distributed continuous or ordinal data were presented as median and interquartile range (IQR). Categorical variables were summarized using frequencies and percentages. Statistical analysis was performed using R [21].. Data was visually tested for normality using histograms. Unpaired Student t-tests were used for normally distributed continuous data. Non-normally distributed continuous and ordinal data were tested using the Wilcoxon–Mann–Whitney tests. Binary categorical data were assessed using chi-squared test with Yates' correction for continuity and non-binary categorical data using the chi-squared test without correction. When expected values were small in 2×2 tables, Fisher's exact test was applied, reporting the p-value as double the exact one-tailed probability. For parameters of interest, odds ratios (OR) and exact 95 % confidence intervals were calculated from the "stats" package in R. The threshold for statistical significance was determined as a p-value of <0.05.

Results

A flowchart of the selection process is presented in Fig. 1. In total, 901 consecutive trauma bay admissions were identified through the clinic information system. Notably, this included only patients with a confirmed informed consent. Of those, 627 patients had to be excluded based on lower injury severity, lack of surgical interventions, or the number of injured body regions. Of the remaining 274 patients, a further 35 were excluded as early total care was performed as primary treatment strategy. Of the remaining 239 patients, 151 patients were allocated to the "Delayed Fracture Care" group (***Group DFC***) and 88 patients were allocated to the "Safe Definitive Surgery" group (***Group SDS***).

Patient demographics and injury specific factors are presented in Table 1. Patient groups did not differ significantly in regard to age and physical status (ASA physical status classification)[22]. There was, however, a significantly lower number of females in ***Group SDS***.

Group DFC had a significantly higher median ISS with a similar number of injured body regions. In regard to physiological stability, lifesaving interventions, and NSI, the percentage was significantly higher in ***Group DFC***. Besides these, no significant differences between the groups were noted in regard to soft tissue- or chest injury.

Primary outcomes are visualized in Fig. 2A**.** One can identify higher OR for SIRS and Sepsis in ***Group DFC***; however these are not significant *($p = 0.181$ and $p = 0.322$ resp.)*. These results suggest that SDS is non-inferior to DFC, despite being the more invasive treatment option. No deaths were noted in either group. Concerning the procedural outcomes, there was a significantly shorter interval until the first definitive and until the final definitive operation in ***Group SDS***, combined with a significantly lower number of total operative interventions (*See* Table 1*; p-values: <0.001, 0.013, and 0.037 resp.*).

Table 2 gives a more in depth overview over the severity of TBI, the different types of IB and the need for NSI. The most relevant factors from Tables 1 and 2 are visualized in the forest plot Fig. 2B. OR for delaying surgery were calculated for each factor and 95 % confidence intervals (95 %CIs) are presented. Unstable physiology is a highly significant indicator for delaying surgery (*OR: 2.85; 95 %CIs: 1.56 to 5.33; $p < 0.001$*). The presence of relevant soft tissue injury and relevant chest injury show no significant effect on delaying fracture care. For the presence of IB (with and w/o NSI), there is a trend towards delaying

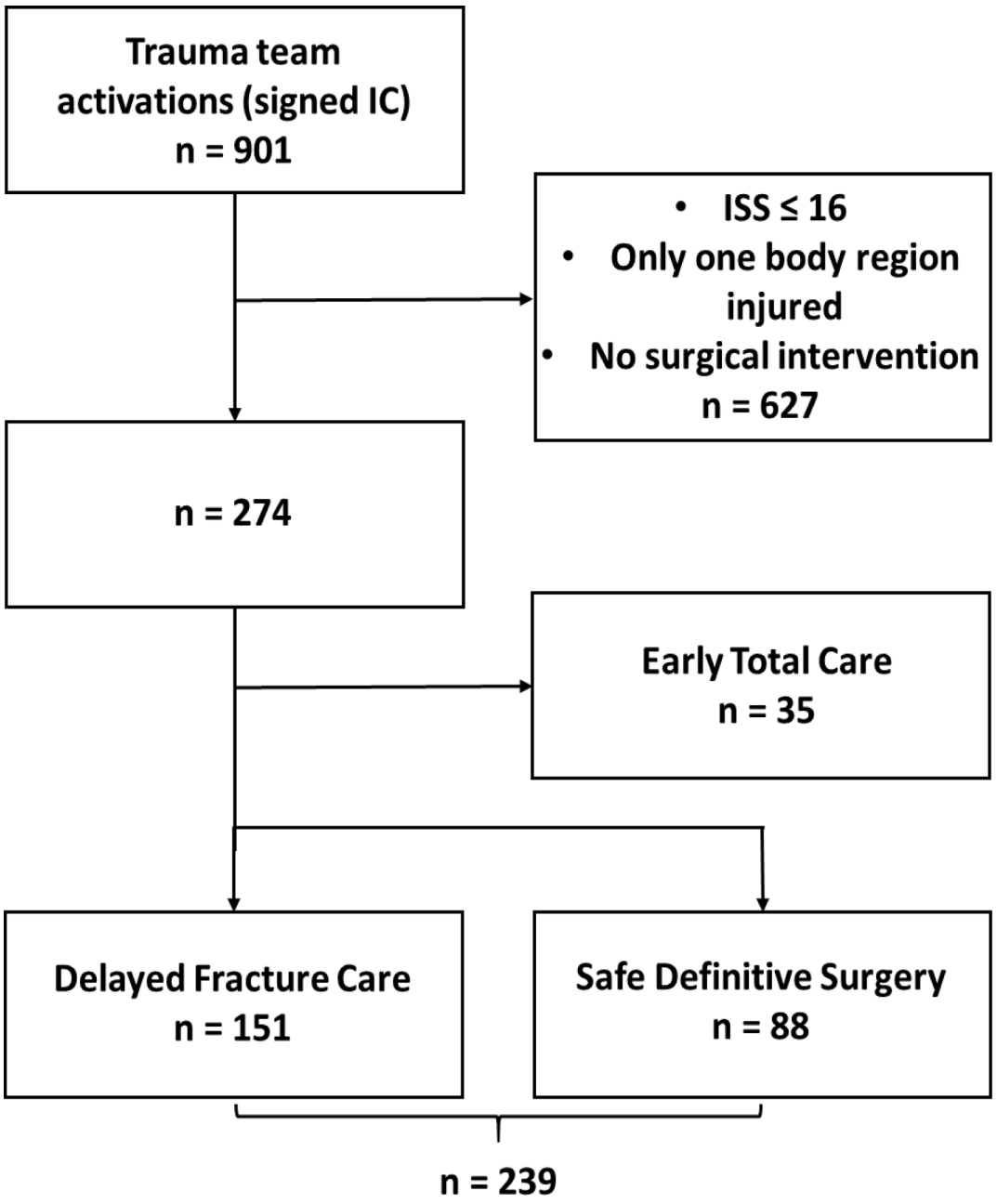

Trauma team activations (signed IC) n = 901
• ISS ≤ 16
• Only one body region injured
• No surgical intervention
n = 627
n = 274
Early Total Care n = 35
Delayed Fracture Care n = 151
Safe Definitive Surgery n = 88
n = 239

Fig. 1. Flowchart of patient selection process, IC = informed consent.

surgery, albeit not significant (*OR: 1.70; 95 %CIs: 0.94 to 3.13; p = 0.081*). In regard to the type of bleeding, intraparenchymal bleedings and epidural hematomas showed a trend for delaying fracture care, although missing the threshold for statistical significance (*OR: 2.26; 95 %CIs: 0.98 to 5.70; p = 0.055 and OR: 6.80; 95 %CIs: 0.96 to 297.17; p = 0.058*). Finally, NSI is a highly significant factor and has the highest odds to delay fracture care *(OR: 5.59; 95 %CIs: 1.63 to 29.85; p = 0.002*). Notably, the presence of IB without NSI does not significantly delay surgery (*OR: 1.21; 95 %CIs: 0.63 to 2.34; p = 0.652)*. Amongst those patients presenting with IB, epidural hematomas and intraparenchymal bleedings have markedly higher odds for NSI, though without statistical significance *(OR: 3.92; 95 %CIs: 0.95 to 17.58; p = 0.06 and OR: 1.84; 95 %CIs: 0.67 to 5.11; p = 0.273)*.

In view of these results and for more comprehensibility, patients were then stratified in three categories based on the presence of IB and the need for NSI (*See* Table 2*: TBI Category*). These categories, while significantly different in regard to the chosen treatment strategy (*p = 0.008 in Chi^2-Test*), clearly show that the percentage of IB without NSI does not differ between the groups (*26 % in both*). Indeed, the odds for delaying surgery in patients with IB, but without the need for NSI are close to one (*OR: 1.21; 95 %CIs: 0.63 to 2.34; p = 0.652)*. This is further emphasized in Fig. 3, visualizing treatment strategies based on patient physiology and TBI category. Apparently, intracranial trauma sequelae that require NSI are highly relevant in both physiologically stable and unstable patients. The presence of IB without NSI does not significantly influence the treatment decision towards delaying fracture care. In patients, who were physiologically stable and who did not receive NSI, the presence of soft tissue injury became a significant factor for delaying definitive surgery (*OR: 2.51; 95 %CIs: 1.09 to 6.02; p = 0.029*). For these patients, the treatment strategy was classified as MuST surgery.

Discussion

The implementation of patient-tailored, physiology-based, dynamic

Table 1
Overview demographics, physiology, concomitant injuries, procedural characteristics, and outcomes. DFC = delayed fracture care, SDS = "Safe Definitive Surgery".

	Overall	Group DFC	Group SDS	p.
Number (n =)	**239**	**151**	**88**	
Demographics				
Age (mean, SD)	45 (19)	45 (19)	45 (18)	0.918
ASA (mean, SD)	1.4 (0.6)	1.4 (0.6)	1.4 (0.5)	0.934
Gender, female (%)	68 (29)	51 (34)	17 (19)	**0.025**
ISS (median, IQR)	24 [20, 33]	27 [22, 34]	22 [19, 27]	**0.044**
Injured body regions (median, IQR)	3 [2, 4]	3 [2, 4]	3 [2, 3]	0.121
Physiology / Stability				
Not stable, *n* (%)	99 (41)	76 (50)	23 (26)	**<0.001**
Livesaving surgery, *n* (%)	46 (19)	38 (25)	8 (9)	**0.004**
Traumatic Brain Injury				
GCS (median, IQR)	14 [12, 15]	14 [10.5, 15]	14 [13, 15]	0.578
Intracranial bleeding, *n* (%)	89 (37)	63 (42)	26 (30)	0.082
Neurosurgical intervention, *n* (%)	28 (12)	25 (17)	3 (3)	**0.002**
Chest Injury				
Relevant chest injury, *n* (%)	171 (72)	109 (72)	62 (71)	0.886
AIS chest (median, IQR)	3 [2, 3]	3 [2, 3]	3 [2, 3]	0.434
Soft Tissue Injury				
Relevant soft tissue injury, *n* (%)	157 (66)	104 (69)	53 (60)	0.224
Open fracture > 1°, *n* (%)	71 (30)	50 (33)	21 (24)	0.173
Neural / vascular injury, *n* (%)	38 (16)	28 (19)	10 (11)	0.200
Procedural				
Days to first operation (mean, SD)	2.9 (3.6)	4.4 (3.7)	0.3 (0.9)	**<0.001**
Days to full reconstruction (mean, SD)	13.2 (13.6)	14.9 (15.6)	10.3 (8.8)	**0.013**
Number of operations (mean, SD)	4.9 (3.3)	5.3 (3.8)	4.3 (2.2)	**0.037**
Outcomes				
Survival for 72 h, *n* (%)	239 (100)	151 (100)	88 (100)	N/A
SIRS, *n* (%)	26 (11)	20 (13)	6 (7)	0.181
Sepsis, *n* (%)	11 (5)	9 (6)	2 (2)	0.322

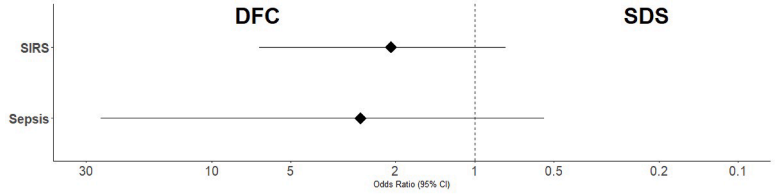
protocols for the treatment of polytrauma patients has been repeatedly shown to improve outcomes, especially in regard to length of hospitalization and duration of rehabilitation[4,6,23]. While the importance of hemorrhage control, coagulation, body temperature, and adequate ventilation is universally accepted and extensively researched, the impact of TBI is less well explored and comprehensive guidelines and recommendations are lacking[1]. While the relevance of TBI for the timing of fracture care is indisputable, the particulars are yet to be determined[14,24]. In this retrospective cohort study of polytrauma patients, NSI and unstable physiology were identified as key factors to influence surgical treatment strategy for reconstruction of major fractures. The main results can be stated as follows:

1. By selecting polytrauma patients based on their physiological response and the severity of their intracranial trauma sequelae, early definitive fracture care could be performed. This lead to significantly fewer surgical interventions, without being associated with early mortality or increased rates of SIRS and Sepsis.
2. Intracranial trauma sequelae requiring NSI are significant factors to delay definitive fracture care in both, physiologically stable and unstable polytrauma patients. The presence of IB without NSI did not show a relevant effect on the surgical strategy.
3. Besides NSI, unstable physiology is the most significant factor to delay definitive fracture care in our cohort. Chest injury did not significantly alter the treatment strategy.

The first result of this study is in line with the published data of the literature in the field and supports the generally accepted opinion that fracture care should be performed as early as possible[25]. Additionally, this retrospective analysis shows that patients in ***Group SDS*** received significantly fewer operations, while full reconstruction was completed significantly earlier. Previous studies have suggested that this might lead to earlier mobilization and thus a reduced length of hospitalization a reduction of (especially pulmonary) complications[4,6,23]. Considering these results, it is reasonable to assume that the allocation to the "Safe

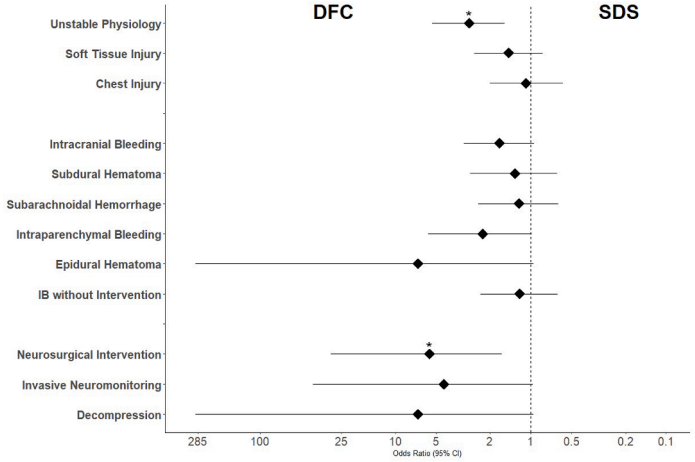
Table 2
Overview of traumatic brain injuries (TBI) including type of intracranial bleeding (IB) and need for neurosurgical intervention (NSI). DFC = delayed fracture care, SDS = "Safe Definitive Surgery".

	Overall	Group DFC	Group SDS	p.
Number (n =)	**239**	**151**	**88**	
Severity of TBI, *n* (%)				0.162
Mild (GCS 13-15)	136 (57)	85 (56)	51 (58)	–
Moderate (GCS 9-12)	25 (11)	14 (9)	11 (13)	–
Severe (GCS 3-8)	37 (16)	29 (19)	8 (9)	–
GCS (median [IQR])	14 [12, 15]	14 [10.5, 15]	14 [13, 15]	0.578
Intracranial Bleeding, *n* (%)	89 (37)	63 (42)	26 (30)	0.081
Epidural, *n* (%)	12 (5.0)	11 (7)	1 (1)	0.073
Subdural, *n* (%)	47 (20)	32 (21)	15 (17)	0.547
Subarachnoid, *n* (%)	57 (24)	38 (25)	19 (22)	0.644
Intraparenchymal, *n* (%)	40 (17)	31 (21)	9 (10)	0.055
Dominant Bleeding, *n* (%)				0.859
Primarily epidural	6 (7)	5 (8)	1 (4)	–
Primarily subdural	19 (21)	14 (22)	5 (19)	–
Primarily subarachnoid	19 (21)	12 (19)	7 (27)	–
Primarily intraparenchymal	9 (10)	7 (11)	2 (8)	–
Multiple	36 (40)	25 (40)	11 (42)	–
NSI, *n* (%)	28 (12)	25 (17)	3 (3)	**0.002**
Invasive neuromonitoring, n (%)	16 (7)	14 (9)	2 (2)	0.057
Decompression, n (%)	12 (5)	11 (7)	1 (1)	0.058
Category of TBI, n (%)				**0.008**
No IB	149 (62)	87 (58)	62 (70)	–
IB w/o NSI	62 (26)	39 (26)	23 (26)	–
NSI	28 (12)	25 (17)	3 (3)	–



	Odds Ratios	Lower 95% CI	Upper 95% CI	p.
SIRS	2.08	0.76	6.60	0.181
Sepsis	2.72	0.54	26.41	0.322

Fig. 2A. . Odds ratios for SIRS and sepsis in relation to the treatment strategy. DFC = delayed fracture care, SDS = "Safe Definitive Surgery".



	Odds Ratios	Lower 95% CI	Upper 95% CI	p.
Unstable Physiology	2.85	1.56	5.33	**<0.001**
Soft Tissue Injury	1.46	0.81	2.62	0.224
Chest Injury	1.09	0.58	2.02	0.886
Intracranial Bleeding	1.70	0.94	3.13	0.081
Subdural Hematoma	1.31	0.64	2.79	0.547
Subarachnoidal Hemorrhage	1.22	0.63	2.43	0.644
Intraparenchymal Bleeding	2.26	0.98	5.70	0.055
Epidural Hematoma	6.80	0.96	297.17	0.058
IB w/o Intervention	1.21	0.63	2.34	0.652
Neurosurgical Intervention	5.59	1.63	29.85	**0.002**
Invasive Neuromonitoring	4.37	0.97	40.60	0.057
Decompression	6.80	0.96	297.17	0.058

Fig. 2B. . Odds ratios for delayed definitive fracture care depending on additional factors with focus on the presence of intracranial trauma sequelae and neurosurgical interventions. DFC = delayed fracture care, SDS = "Safe Definitive Surgery", IB = intracranial bleeding.

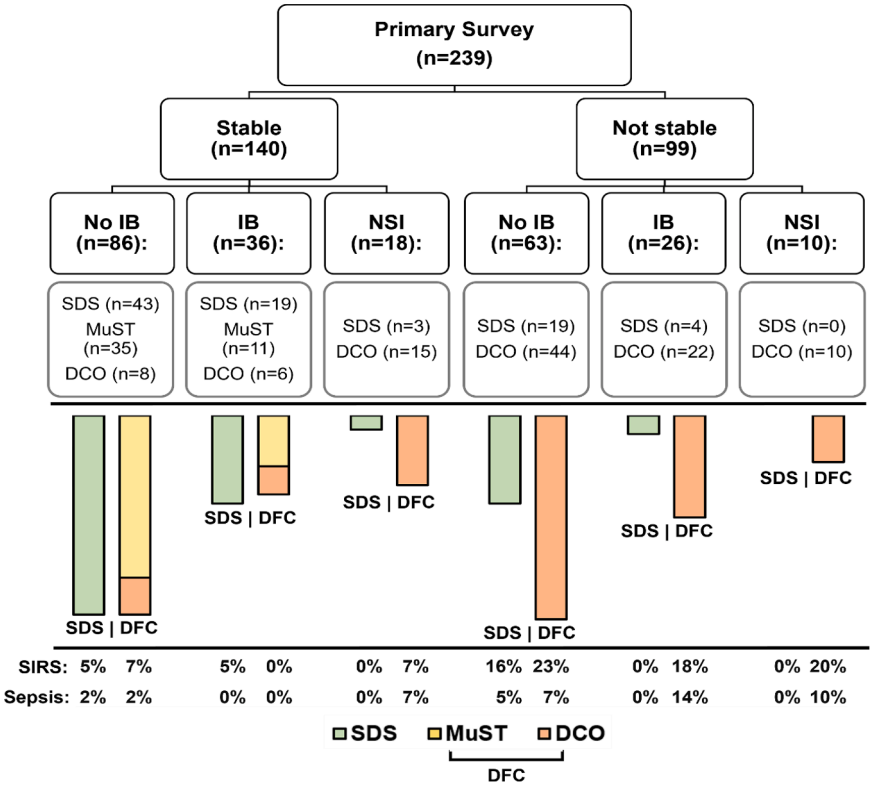


Fig. 3. Flowchart, bar chart and table visualizing the treatment strategies and outcomes based on patient physiology, presence of intracranial bleeding (IB) (without operation) and intracranial trauma sequelae with the need for neurosurgical intervention (NSI). The bars indicate the number of patients receiving SDS and DFC (DCO + Must). The percentage of SIRS and Sepsis is indicated for the respective groups.
SDS = Safe Definitive Surgery, DFC = Delayed Fracture Care, DCO = damage control orthopaedics, MuST = "MusculoSkeletal Temporary Surgery".

Definitive Surgery" group was performed based on sound criteria, thus substantiating the second and third major finding. In regard to the correct identification of patients, who might benefit from "Safe Definitive Surgery", a summary parameters and thresholds was recently published[17].

Our second major finding points to the importance of NSI, or more precisely, trauma sequelae that require NSI, as the most relevant intracranial factors to delay definitive fracture care. In this cohort, this included patients, who underwent more invasive approaches including craniotomies or decompressive craniectomies but also minor invasive procedures such as insertions of external ventricular drainages and invasive neuromonitoring. As previously stated, the indication for these operations usually are relevant mass lesions and signs of increased intracranial pressure (ICP), which are frequently associated with unfavorable outcomes as reported in the literature[26–28]. Indeed, several previous publications on severe TBI focus on either the presence of a MLS $>$ 5 mm, or an increased ICP and decreased cerebral perfusion pressure as indicative of mortality and complications[20,26–28]. The invasive measurement of an ICP prerequisites that a NSI has already been carried out. A MLS $>$ 5 mm on the other hand is usually one of the morphological indications for NSI according to the guidelines published by neurosurgical societies[20]. Therefore, the results of this study could be considered in line with the published literature. Nevertheless, studies on the surgical treatment strategies in polytrauma patients with TBI are rare. In a previous work, our group was able to prove a significant association between severe TBI and delaying definitive fracture care, independent of the physiological status[14]. The severity of TBI, however, is typically classified by the GCS, can be biased by several factors, such as intubation, medication, or intoxication[15]. The findings of this current study are primary based on cCT findings, which are more sensitive, specific, and objectively verifiable regarding intracranial pathologies than many clinical findings. They demonstrate that the presence of IB alone, does not necessarily dictate a delay of definitive fracture care. The necessity for NSI, on the other hand, is a highly relevant factor in determining the treatment strategy. Recently, the large Brain vs Bone multicenter trial of the EAST, which included multiply injured patients with diaphyseal femur or tibia fractures and TBI, indicated that the outcome is associated with the initial injury severity, rather than with the timing of the fracture fixation in those patients[24]. While in principle these findings align with the current study, one should still advocate careful individual assessment of each individual case. In patients, who have signs of compensated ICP on cCT without the indication to perform NSI (yet), close follow-up cCT examinations and repeat clinical evaluations are reasonable and the treatment strategy should be adapted accordingly. Prior to the surgical reconstruction of musculoskeletal injuries, risks for peri-operative secondary brain injury should be taken into consideration[25]. Severe blood loss, hemodynamic instability, cerebral hypoperfusion, and hypothermia should be avoided, and patient positioning needs to be taken into consideration. Thus, if possible, percutaneous techniques, minimal invasive procedures, and short operation times are advisable in these cases.

Regarding the third main outcome, the importance of unstable physiology for surgical treatment strategy is generally uncontested[9,29]. Indeed, restoration and protection of oxygenation and end organ perfusion is the fundamental objective in the treatment of trauma patients, which is also clearly reflected in the current data. Therefore, for the sake of this study, life-saving surgery of thorax, abdomen, and pelvis (e.g., emergency thoracotomy / laparotomy for hemorrhage control) were also classified under this parameter. Considering the role of soft tissue injury, there is general agreement that severe soft tissue injury should not be primarily treated with open reconstruction[13,30]. The authors strongly advocate that the local treatment strategy should be dictated by the soft tissue status, which is also confirmed in this current studies data: It shows, that in hemodynamically stable patients who do not require NSI, the presence of soft tissue injury becomes a significant factor, which influences the treatment strategy. In physiologically stable patients with multiple fractures and without the need for NSI, SDS should only be considered for body regions with sound soft tissues.

To summarize, this study was able to identify relevant factors that might help to facilitate treatment algorithms for the fracture care in polytrauma patients with TBI. One such possible algorithm is visualized in Fig. 4: Upon arrival the primary survey should be performed according to the ALTS principles and physiologic stability should be assessed according to existing protocols[17,29]. Patients, who are hemodynamically unstable should be (surgically) resuscitated and repeatedly reassessed. If the patient sufficiently stabilizes to allow further diagnostics such as cCT examinations, the further treatment strategy might be co-determined by the intracranial findings. In hemodynamic stable patients, without the necessity for NSI, SDS can be considered. However, risk for secondary brain injury needs to be evaluated depending on surgical intervention planed. Further factors to be taken into consideration are progression of trauma sequelae in follow-up cCT-scans or deterioration of neurological status[25]. In physiologically stable patients, who require NSI, further treatment strategies should be determined by the intra- and postoperative findings such as signs of elevated ICP and results of follow-up cCT examinations. In physiologically unstable patients, who require NSI, early definitive fracture care is generally not advisable. It is evident that the proposed algorithm has not yet been sufficiently proven in prospective clinical cohorts, which are strongly desired.

Strengths and limitations

This is a retrospective study with the associated limitations regarding potential individual and/or institutional biases. Furthermore, there are some other important potential limitations which need to be discussed. One is the necessity of an informed consent, which is mandatory for the use and export of patient data from this clinic's information system. Typically, this consent has already been obtained during prior hospitalization and is therefore still valid for the purpose our study. However, there is potential of having missed patients who died during hospitalization and had not previously agreed to or rejected the use of anonymized patient data for research purposes. Despite this limitation, we were able to include a relatively large number of patients, all of which had complete data sets. Furthermore, one can argue that complications and further outcome parameters might have supported the validity of this study's results. These outcomes, however, are dependent on multiple patient specific and injury specific factors and should therefore only be investigated with optimized and less heterogeneous patient populations as the ones used in the current study. The included outcome parameters in this cohort were primarily used to support the assumption, that the allocation the "Safe Definitive Surgery" group did not worsen the outcome by creating an insurmountable second hit.

Conclusion

Our results point out that unstable physiology and the necessity of NSI are highly significant factors for delaying definitive fracture care in polytrauma patients, while the presence of intracranial trauma sequelae without intervention had less impact on the timing of definitive fracture care. In physiologically stable patients without NSI, who are closely observed and repeatedly assessed, SDS might be a reasonable strategy to allow timely definitive fracture care. In our cohort, this strategy was not associated with increased patient morbidity. These results could be helpful to clear patients for earlier definitive surgery and should be further investigated in prospective clinical trials.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the ethical committee of the Kanton Zürich, Switzerland (BASEC-Nr. 2020-00703).

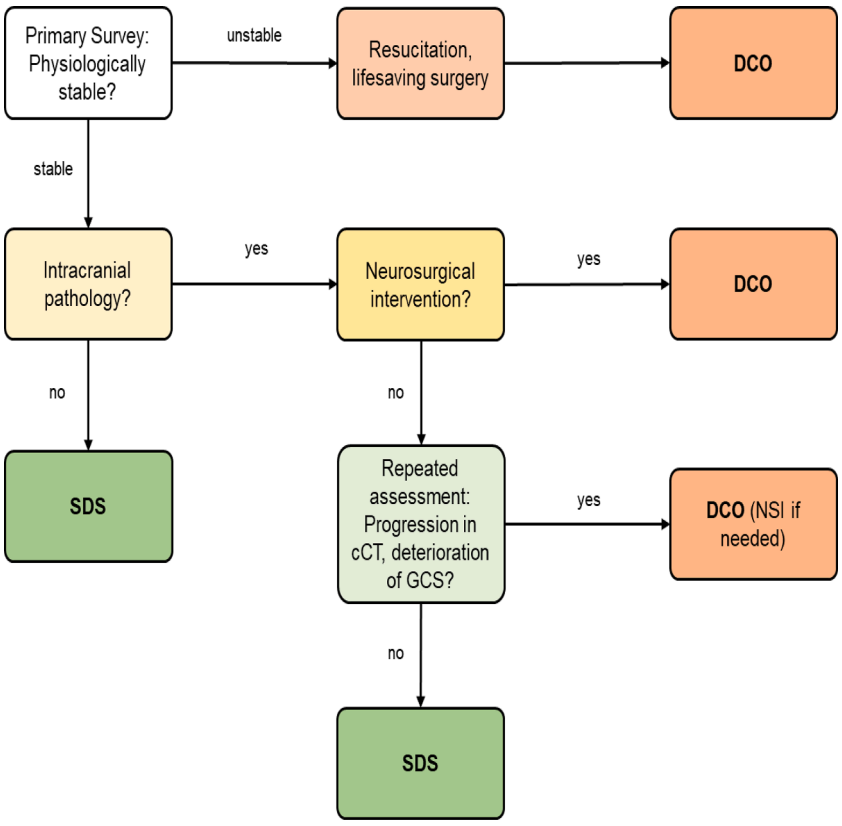


Fig. 4. Proposed treatment algorithm. In stable patients with intracranial trauma sequelae, treatment strategy should be based on repeated assessments and cCT. The risk for secondary brain injury, neurologic deterioration, and progression of bleeding needs to be always considered. DCO = damage control orthopaedics, SDS = "Safe Definitive Surgery".

CRediT authorship contribution statement

Yannik Kalbas: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Yannik Stutz:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Data curation. **Felix Karl-Ludwig Klingebiel:** Writing – review & editing, Visualization, Methodology, Data curation. **Sascha Halvachizadeh:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Michel Paul Johan Teuben:** Writing – review & editing, Visualization, Methodology, Investigation, Conceptualization. **John Ricklin:** Writing – review & editing, Methodology, Data curation. **Ivan Sivriev:** Data curation, Conceptualization. **Jakob Hax:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Carlos Ordonez Urgiles:** Writing – review & editing, Methodology, Data curation. **Kai Oliver Jensen:** Writing – review & editing, Investigation, Conceptualization. **Markus Florian Oertel:** Writing – review & editing, Supervision, Conceptualization. **Hans-Christoph Pape:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Roman Pfeifer:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Newcombe VFJ, Chow A. The features of the typical traumatic brain injury patient in the ICU are changing: what will this mean for the intensivist? Curr Opin Crit Care 2021;27(2):80–6.
[2] Pfeifer R, Tarkin IS, Rocos B, Pape HC. Patterns of mortality and causes of death in polytrauma patients–has anything changed? Injury 2009;40(9):907–11.
[3] Bone LB, Johnson KD, Weigelt J, Scheinberg R. Early versus delayed stabilization of femoral fractures. A prospective randomized study. J Bone Joint Surg Am 1989;71(3):336–40.
[4] Nahm NJ, Como JJ, Wilber JH, Vallier HA. Early appropriate care: definitive stabilization of femoral fractures within 24 h of injury is safe in most patients with multiple injuries. J Trauma 2011;71(1):175–85.
[5] Giannoudis PV, Giannoudis VP, Horwitz DS. Time to think outside the box: 'Prompt-Individualised-Safe Management' (PR.I.S.M.) should prevail in patients with multiple injuries. Injury 2017;48(7):1279–82.
[6] Pape HC, Halvachizadeh S, Leenen L, Velmahos GD, Buckley R, Giannoudis PV. Timing of major fracture care in polytrauma patients - An update on principles, parameters and strategies for 2020. Injury 2019;50(10):1656–70.
[7] Pape HC, Pfeifer R. Safe definitive orthopaedic surgery (SDS): repeated assessment for tapered application of early definitive care and damage control?: An inclusive view of recent advances in polytrauma management. Injury 2015;46(1):1–3.
[8] Vallier HA, Wang X, Moore TA, Wilber JH, Como JJ. Timing of orthopaedic surgery in multiple trauma patients: development of a protocol for early appropriate care. J Orthop Trauma 2013;27(10):543–51.
[9] Kalbas Y, Heining SM, Kaiser A, Klingebiel FK, Pfeifer R, Wanner GA, Pape HC. Fracture fixation in polytraumatized patients-from an interdisciplinary early total/appropriate care to the safe definitive surgery concept. Front Med (Lausanne) 2024;11:1362986.
[10] Halvachizadeh S, Baradaran L, Cinelli P, Pfeifer R, Sprengel K, Pape HC. How to detect a polytrauma patient at risk of complications: a validation and database analysis of four published scales. PLoS One 2020;15(1):e0228082.
[11] Rossaint R, Afshari A, Bouillon B, Cerny V, Cimpoesu D, Curry N, et al. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. Crit Care 2023;27(1):80.
[12] Kalbas Y, Klingebiel FK, Halvachizadeh S, Kumabe Y, Scherer J, Teuben M, et al. Developments in the understanding of staging a "major fracture" in polytrauma: results from an initiative by the polytrauma section of ESTES. Eur J Trauma Emerg Surg 2023.

[13] Pfeifer R, Kalbas Y, Coimbra R, Leenen L, Komadina R, Hildebrand F, et al. Indications and interventions of damage control orthopedic surgeries: an expert opinion survey. Eur J Trauma Emerg Surg 2021;47(6):2081–92.
[14] Halvachizadeh S, Pfeifer R, Duncan J, Klingebiel FKL, Kalbas Y, Berk T, et al. Does the injury pattern drive the surgical treatment strategy in multiply injured patients with major fractures? J Trauma Acute Care Surg 2024.
[15] Reith FC, Synnot A, van den Brande R, Gruen RL, Maas AI. Factors influencing the reliability of the Glasgow coma scale: a systematic review. Neurosurgery 2017;80 (6):829–39.
[16] Pape HC, Moore EE, McKinley T, Sauaia A. Pathophysiology in patients with polytrauma. Injury 2022;53(7):2400–12.
[17] Pfeifer R, Klingebiel FK, Halvachizadeh S, Kalbas Y, Pape HC. How to clear polytrauma patients for fracture fixation: results of a systematic review of the literature. Injury 2023;54(2):292–317.
[18] Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am 1976;58(4):453–8.
[19] Kalbas Y, Pape HC. What factors determine a "major fracture"? Injury 2022;53(8): 2701–3.
[20] Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Guidelines for the management of severe traumatic brain injury. Fourth Edition Neurosurgery 2017;80(1):6–15.
[21] R Core Team (2022) R: a language and environment for statistical computing. R foundation for statistical computing, Vienna, Austria. URL https://www.R-project.org/.
[22] Skaga NO, Eken T, Søvik S, Jones JM, Steen PA. Pre-injury ASA physical status classification is an independent predictor of mortality after trauma. J Trauma 2007;63(5):972–8.
[23] Vallier HA, Cureton BA, Ekstein C, Oldenburg FP, Wilber JH. Early definitive stabilization of unstable pelvis and acetabulum fractures reduces morbidity. J Trauma 2010;69(3):677–84.
[24] Ghneim M, Kufera J, Zhang A, Penaloza-Villalobos L, Swentek L, Watras J, et al. Does lower extremity fracture fixation technique influence neurologic outcomes in patients with traumatic brain injury? The EAST brain vs. bone multicenter trial. J Trauma Acute Care Surg 2023;95(4):516–23.
[25] Pfeifer R, Klingebiel FK-L, Balogh ZJ, Beeres FJP, Coimbra R, Fang C, et al. Early major fracture care in polytrauma—priorities in the context of concomitant injuries: a Delphi consensus process and systematic review. J Trauma Acute Care Surg 2024;97(4):639–50.
[26] Lannoo E, Van Rietvelde F, Colardyn F, Lemmerling M, Vandekerckhove T, Jannes C, De Soete G. Early predictors of mortality and morbidity after severe closed head injury. J Neurotrauma 2000;17(5):403–14.
[27] Jiang JY, Gao GY, Li WP, Yu MK, Zhu C. Early indicators of prognosis in 846 cases of severe traumatic brain injury. J Neurotrauma 2002;19(7):869–74.
[28] Schreiber MA, Aoki N, Scott BG, Beck JR. Determinants of mortality in patients with severe blunt head injury. Arch Surg 2002;137(3):285–90.
[29] Advanced trauma life support (ATLS®): the ninth edition. J Trauma Acute Care Surg 2013;74(5):1363–6.
[30] Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, et al. Fracture-related infection: a consensus on definition from an international expert group. Injury 2018;49(3):505–10.